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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/852,666	05/07/97	CHADA	K UAB-1.0-0370

HM11/1027

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EXAMINER	
SRIVASTAVA,P	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/27/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/852,666	Applicant(s) Chada et al.
	Examiner Devesh Srivastava, Ph.D.	Group Art Unit 1652

☒ Responsive to communication(s) filed on *Sep 14, 1998* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-40* is/are pending in the application.

Of the above, claim(s) *1-5, 13-15, 20-22, 26-28, and 33-40* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *6-12, 16-19, 23-25, and 29-32* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The Art Unit location of the instant application has changed. To aid in correlating any papers for this application, all further correspondence regarding this application and the elected claims should be directed to Group Art Unit 1652, Technology Center 1600/2900.

Election/Restriction

1. Applicant's election with traverse of the claims of Group V: claims 6-12, 16-19, 23-25 and 29-32 in Paper No. 5 is acknowledged. The traversal is on the ground(s) that the search and examination of the instant application can be made without serious burden to the examiner because groups II, IV, VI and VII are classified in Class 435 and groups III and V are classified in Class 514. This is not found persuasive because the aforementioned groups have been classified among two major classes and they are further classified in 5 different subclasses. Ggroup I is further classified in Class 800 which is even more divergent than the classification of the 6 other groups. Finally, the divergent subject matter would require different, non-overlapping searches for each group.

The requirement is still deemed proper and is therefore made FINAL.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The first inventor's signature lacks the middle initial, therefore it does not match the typed name.

The full name of each inventor (family name and at least one given name together with any initial) has not been set forth.

The full given name of the inventor, Hena Ashar, is not set forth. Based on the specification (page 8, line 14) and published manuscripts, it appears that the inventor's full given name is Hena R. Ashar.

The full given name of the inventor, Alex Tkachenko, is not set forth. Based on published manuscripts, it appears that the inventor's full given name is Alexei Tkachenko.

Specification

3. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 250 words. It is important that the abstract not exceed 250 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract is greater than 250 words in length and needs to be reduced.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 6-12 and 16-19 provide for the use of reduction in biological activity of HMGI genes, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

6. Claims 23-25 and 29-32 provide for the use of regulation of growth and development of adipose tissue, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

7. Claims 16 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Both claims recite "*inhibiting the protein-protein interactions of HMGI proteins*" (page 65, lines 24-25 and page 67, lines 5-6, respectively). Neither the claims nor the specification define "*protein-protein interactions*" and therefore, it is impossible to define the metes and bounds of this phrase.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 6-12, 16-19, 23-25 and 29-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Claims 6-12 and 16-19 recite methods for treating obesity in mammals. According to the specification, the mammal may be human or rodent (page 11, lines 18-19). The specification also discloses: "*The reduction in biological activity of HMGI genes may be achieved by inhibiting the DNA-binding activity of HMGI genes which may be carried out by administering to the mammal a therapeutically effective amount of netropsin, distamycin A or Hoechst 33258*

(bisbenzimide)." (page 11, lines 13-16). The specification fails to disclose the composition in which any of the three drugs will be administered, the frequency of administration, the need for coincidental changes in behaviour including diet and exercise or the effect of confounding factors such as diabetes. Since these drugs are not known in the art to reduce the *in vivo* activity of HMGI proteins, it can not be predicted if such a reduction would occur. The specification further discloses: "*The reduction in biological activity of HMGI genes may be achieved by inhibiting the expression of HMGI genes which may be carried out by administering to the mammal a therapeutically effective amount of an oligonucleotide which has a nucleotide sequence complementary to at least a portion of the mRNA of the HMGI gene.*" (page 11, lines 9-13). The specification has only general statements concerning the frequency, dosage, mode and site(s) of administration of antisense oligonucleotides and leaves these factors to be determined "*in accordance with conventional practice among medical or veterinary professionals*" (page 53, lines 6-7). Claim 16 recites inhibiting protein-protein interactions of HMGI proteins. It is known that HMGI proteins regulate gene expression by functioning as architectural factors to induce conformational changes in DNA. However, the specification fails to disclose how the inhibition of protein-protein interactions of HMGI proteins would be accomplished as well as what compounds would be used to accomplish this goal.

With respect to claims 6-12 and 16-19, Marx states that "*Few medical problems have proved to be more intractable than obesity*" (page 1477, column 1, , lines 1-2) and Rink states

"...*much remains to be done*" towards therapeutic approaches to obesity (page 407, column 2, line 12).

With respect to antisense oligonucleotide approaches to reduce biological activity of HMGI genes, Branch states "*the antisense field has been turned on its head by the discovery of 'non-antisense' effects, which occur when a nucleic acid drug acts on some molecule other than its intended target*" and this "*unpredictability confounds research applications of nucleic acid reagents.*" (page 45, column 2, lines 3-7 and 13-15). Branch further states "*internal structures of target RNAs and their associations with cellular proteins create physical barriers, which render most potential binding sites inaccessible to antisense molecules.*" (page 45, column 3, lines 1-5). The latter point illustrates the need for antisense oligonucleotides that are complementary to exposed regions of target RNA. It is unclear if the disclosed antisense oligonucleotides are complementary to exposed regions of target RNA.

The art, as referenced above, suggest that there is much more to be done before effective treatments for obesity can be performed. Further, given the unpredictability in the art, there is also a lack of a working example in the specification. Specifically, there is no example of a reduction in biological activity of an HMGI protein in a mammal that is produced by either of the disclosed methods quoted above.

In view of the unpredictability in the arts of treating obesity and antisense oligonucleotide technology, the lack of clear guidance with respect to dosage and frequency of administration of

drugs or antisense oligonucleotides and the lack of a working example, one skilled in the art could not use the inventions of claims 6-12 and 16-19 without undue experimentation.

Claims 23-25 and 29-32 recite methods for regulating growth and development of adipose tissue in a mammal.. According to the specification, the mammal may be human or rodent (page 11, lines 18-19). See discussion above for disclosed methods by which this would be accomplished as well as the discussion of why the art of antisense technology is unpredictable.

With respect to claims 23-25 and 29-32, HMGI proteins are suggested to play a role in adipogenesis (Guerre-Millo et al. and Auwerx et al.). However, Guerre-Millo et al. state "*Although major progress has been made into clarifying the basic role of transcription factors in adipocyte differentiation, major challenges lie ahead before this can be extrapolated to the human situation.*" (page 1530, column 1, lines 20-23) and Auwerx et al. state "*...studies should be designed to test whether results obtained using animal models and in vitro cell culture systems can be extrapolated to the human situation and eventually applied in medical practice. Although enormous progress has been made regarding the role which transcription factors play in adipocyte differentiation, major challenges lie ahead.*" (page 350, column 2, lines 1-7).

The art, as referenced above, suggest that there is much more to be done before effective regulation of growth and development of adipose tissue (adipogenesis) can be performed. Further, given the unpredictability in the art, there is also a lack of a working example in the specification. Specifically, there is no example of a reduction in biological activity of an HMGI protein in a mammal that is produced by either of the disclosed methods.

In view of the unpredictability in the arts of regulating adipogenesis and antisense oligonucleotide technology, the lack of clear guidance with respect to dosage and frequency of administration of drugs or antisense oligonucleotides and the lack of a working example, one skilled in the art could not use the inventions of claims 23-25 and 29-32 without undue experimentation.

Claims 16 and 29 recite inhibiting protein-protein interactions of HMGI proteins. It is known that HMGI proteins regulate gene expression by functioning as architectural factors to induce conformational changes in DNA, however, the specification fails to disclose how the inhibition of protein-protein interactions of HMGI proteins would be accomplished.

Conclusion

10. Claims 1-5, 13-15, 20-22, 26-28 and 33-40 are withdrawn from consideration as being non-elected claims.

11. Claims 6-12, 16-19, 23-25 and 29-32 are rejected.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Devesh Srivastava, Ph.D. whose telephone number is (703) 305-0775. The

examiner can normally be reached on Monday-Thursday and alternate Fridays from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Wax, can be reached on (703) 308-4216. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600